

## **REMARKS**

Claims 1 to 3 are in the case.

### **Objections/Informalities**

The Examiner has objected to the abstract. Applicants have submitted a revised abstract. Please see Exhibit A.

The Examiner has maintained the objection to the Specifications suggesting correction of the trademark "PLURONIC" in accordance with M.P.E.P. 608.01(v). The Examiner has noted that Applicants requested that the substitution of "Pluronic®" or "Pluronic" for "PLURONIC®" be done by Examiner's amendment to page 26, in the Table, to page 27 in the Table, to page 27, lines 25 and 40 and to page 28, lines 3 and 23 after the Examiner has indicated that the claims are allowable.

### **Double Patenting Rejection**

The Examiner maintained the rejection of claims 1-3 under the non-statutory doctrine of double patenting over claims 1-4 of US 6,171,801 and claims 1, 2, 4, 5, 10, 11, 26 and 27 of US 6,159,698. The Examiner has noted that Applicants have assured the Office that it will file a terminal disclaimer once the claims are deemed allowable.

### **Rejections under 35 U.S.C. §103(a)**

The Examiner has withdrawn the rejection of claims under §103 as being unpatentable over Nishijo *et al.* or Kaufman *et al.* in view of Neumann *et al.* or Khanna *et al.* (Khanna).

The Examiner has rejected claims 1-3 as being unpatentable over Tabachnick *et al.* (Tabachnick) in view of Khanna.

The Examiner states that Tabachnick teaches a method for releasing or displacing thyroxine (a ligand) from a complex with human serum albumin (endogenous protein) by contacting a medium containing the complex with an effective amount of a substituted benzoic acid derivative, including an *ortho* substituent (which Applicants disclose in the specification as the preferred position for their releasing agents). The Examiner notes that the substituent contains an alkyl group. The Examiner notes that Tabachnick does not teach the use of the specific benzoic acid substituent species recited in the instant claims.

The Examiner states that the use of the specific substituted benzoic acid, methoxybenzoic acid was taught by Khanna to be a releasing agent for releasing a ligand from solution. The Examiner concludes that it would have been obvious to replace Tabachnick's substituted benzoic acid releasing agent with Khanna's specific methoxybenzoic acid releasing agent to produce the method of the instant invention. The Examiner states substitution of one substituted benzoic acid releasing agent with an alternate art-known specific benzoic acid substituent releasing agent would have been well within the realm of routine experimentation. Thus, the Examiner states the claims are *prima facie* obvious over the cited art.

Applicants respectfully traverse the rejection. Contrary to the Examiner's position, Tabachnick teaches that *ortho* substituted benzoic acid derivatives do not work to displace thyroxine from albumin. Specifically, in the abstract: "Bulky halogen atoms *ortho* to the carboxylate group caused **large reductions** in relative binding affinities of benzoates." (emphasis added). See also Table II comparing o-iodo benzoate. Instead, Tabachnick recommends extensive substitution by halogens and particularly at the 3, 4, 5 or 3, 5 positions. See Table II. Furthermore, Tabachnick specifically states that with the effect of

binding of phenols, alkyl substituents are least preferred. Thus, nothing in Tabachnick suggests or discloses uses Applicants the releasing agents used in Applicants' method. Further, as to the preferred embodiment or the present invention, Tabachnick teaches completely away from Applicants' method.

Given that Tabachnick fails to disclose or suggest Applicants method and in fact teaches away from the preferred embodiment, one skilled in the art would not look to Khanna for a specific releasing agent that is a benzoate derivative having a substituent at the *ortho* position or the specific releasing agents recited in the present invention. Further, Khanna does not even teach or suggest a method to release a ligand from an endogenous protein.

Thus, the present invention is not obvious over the combination cited by the Examiner. and Applicants respectfully request reconsideration and withdrawal of the rejection.

For all of the foregoing reasons Applicants respectfully requests that the objections and the rejections of the Examiner be withdrawn and that allowance of the claims be granted. If the Examiner believes that an interview would help to clarify any issue, the Applicants respectfully invite the Examiner to contact Applicants' attorney at the phone number listed below.

Respectfully submitted,



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## Exhibit A

The abstract has been amended as follows:

The present invention relates to a method for releasing a ligand from a complex of the ligand with an endogenous protein using a releasing agent. ~~The releasing agent is an effective amount of a benzoic acid derivative.~~